CARDIOVASCULAR MEDICINE

CLimate Impacts on Myocardial infarction deaths in the Athens TErritory: the CLIMATE study

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Objective: To evaluate the impact of meteorological variables on daily and monthly deaths caused by acute myocardial infarction (AMI).
Methods: All death certificate data from the Athens territory were analysed for AMI deaths in 2001. Daily atmospheric temperature, pressure and relative humidity data were obtained from the National Meteorological Society for Athens for the same year.
Results: The total annual number of deaths caused by AMI was 3126 (1953 men) from a population of 2 664 776 (0.117%). Seasonal variation in deaths was significant, with the average daily AMI deaths in winter being 31.8% higher than in summer (9.89 *v* 7.35, $p < 0.001$). Monthly variation was more pronounced for older people (mean daily AMI deaths of people older than 70 years was 3.53 in June and 7.03 in December; $p < 0.001$) and of only marginal significance for younger people. The best predictor of daily AMI deaths was the average temperature of the previous seven days; the relation between daily AMI deaths and seven-day average temperature ($R^2 = 0.109$, $p < 0.001$) was U-shaped. Considering monthly AMI death rates, only mean monthly humidity was independently associated with total deaths from AMI ($R^2 = 0.541$, $p = 0.004$).
Conclusion: Ambient temperature is an important predictor of AMI mortality even in the mild climate of a Mediterranean city like Athens, its effects being predominantly evident in the elderly. Mean monthly humidity is another meteorological factor that appears to affect monthly numbers of AMI deaths. These findings may be useful for healthcare and civil protection planning.

The environmental effect on the manifestation of cardiovascular disease consists in a multifactorial set of parameters interacting with cardiovascular anatomy and physiology. The contribution of climatic conditions to this effect has been recognised by several studies indicating a seasonal variation of cardiovascular disease morbidity rates and mortality, with events almost consistently showing peaks in winter and troughs in summer,[1–10] although increased incidence of cardiac events during warm weather has been reported.[11–14] Several groups have investigated correlations with specific meteorological variables, the most consistent finding being the relation between ambient temperature and event rates,[15–20] showing in most cases a U-shaped correlation. Results concerning other meteorological factors, such as atmospheric pressure and humidity, have been inconsistent.[15–17 20 21] The objective of the present study was to investigate the seasonal variation of acute myocardial infarction (AMI) deaths and the relation between certain meteorological variables and cardiovascular mortality.

METHODS

Study population

We analysed all the death certificate data from the Athens territory (population of reference: 2 664 776) for death caused by AMI (*International classification of diseases*, 10th revision codes I21.0–4, I21.9, I22.0, I22.1, I22.8 and I22.9) for the year 2001. Mortality data were provided by the National Statistics Service. The cause of death is filled in by the doctor providing the certificate, usually a doctor who knows the deceased person's health status and history or, in the case of a hospitalised patient, the attending doctor of the institution, or by the coroner performing the autopsy when one is deemed necessary. In the second and third case the cause of death is usually recorded with satisfactory accuracy, whereas in the first case, there is room for mistakes due, for instance, to incorrect diagnosis of the cause of death or inadequate completion of the death certificate. However, the error originating from such problems is not likely to have any seasonal differentiation or relation to climatic conditions and, thus, we did not expect it to cause systematic errors. Our reference population was 2 664 776, according to the data provided by the National Statistics Service. The vacation period for Athenians is limited to 30 days from late July to late August, during which the reference population may be decreased. However, as pointed out in the results section, the observed minimum in AMI deaths was in June, which is not a month of holidays for the residents of Athens. This indicates that the observed variations in AMI deaths are probably not attributable to variations in the reference population.

Meteorological data

Daily mean, minimum and maximum atmospheric temperatures (℃), daily mean atmospheric pressure (millibars) and daily mean relative humidity (percentage) were obtained from the National Meteorological Society for the Athens territory and for the same year. Seasons were defined by their calendar notion (winter: 1 January to 28 February and 1–31 December; spring: 1 March to 31 May; summer: 1 June to 31 August; and autumn: 1 September to 30 November).

Statistical analysis

Data are presented as mean (SD). The two-sided t test was used to compare the means of continuous variables. The χ^2 test was used to compare categorical values and percentages. Values of $p < 0.05$ were considered significant. We applied

Abbreviations: AMI, acute myocardial infarction; MONICA, MONitoring trends and determinants In CArdiovascular disease; PM, particulate matter

Table 1 Seasonal distribution and daily averages of acute myocardial infarction deaths for each season and the 12-month period of evaluation

	Winter		Spring		Summer		Autumn		Total	
	No	Mean	No	Mean	No	Mean	No	Mean	No	Mean
Men	544	6.05 (2.57)	499	5.42 (2.49)	444	4.83 (1.92)	466	5.12 (2.18)	1953	5.35 (2.34)
Women	346	3.84 (1.97)	311	3.38 (1.83)	232	2.52 (1.79)	284	3.12 (1.92)	1173	3.21 (1.93)
Total	890	9.89 (3.48)	810	8.80 (3.12)	676	7.35 (2.88)	750	8.24 (2.86)	3126	8.56 (3.21)

Data are mean (SD).

multiple linear and non-linear regression analysis models to assess the effect of each meteorological variable on the daily number of AMI deaths. The best fit was judged on the basis of the residual sum of squares and the value of the R^2 statistic. All meteorological variables were entered in the model as independent variables, as well as the mean values of the previous seven days. As there is no physiological reason to select one time lag over another and because in the past different authors have used several time lags for the effect of temperature on mortality,[18 19] we chose to include only the seven-day lag in our analysis, as other investigators have done,[20] also trying to avoid an inadvertent increase in the number of variables leading to possible false correlations due to multiple comparisons. For the analysis of monthly mortality and meteorological data we used a simple model of forward linear regression analysis. Data were analysed with the SPSS V.10.0 statistical package for Windows (SPSS Inc, Chicago, Illinois, USA).

RESULTS

During the 12 months of the study (January through December 2001) 3126 (1173 women, 37.5%) deaths were recorded in the Athens area with AMI as the primary cause of death (annual AMI mortality rate 1.17/1000). The annual mean daily number of AMI deaths was 8.56 (SD 3.21).

The lowest recorded temperature was 1℃ on 18, 19 and 24 December and the highest was 39℃ on 9 and 10 August. For mean daily relative humidity, the maximum was 91%, recorded on 5 November, and the minimum was 26%, recorded on 9 August. Mean daily atmospheric pressure maximum and minimum values were 1030 mbars and 1001 mbars, on 10 December and 26 February, respectively. The highest monthly mean maximum temperature was 34.3℃ in August and the lowest monthly mean minimum temperature was 5.9℃ in December. The most humid month was December (mean relative humidity 72.6%) and the driest was August (43.6%).

Table 2 Monthly counts and daily averages of acute myocardial infarction (AMI) deaths for each month

Month	No of AMI deaths	Daily average
January	302	9.74 (2.93)
February	257	9.18 (2.98)
March	284	9.16 (3.38)
April	276	9.20 (2.58)
May	250	8.06 (3.29)
June	185	6.17 (2.07)
July	247	7.97 (3.42)
August	244	7.87 (2.68)
September	248	8.27 (3.24)
October	230	7.42 (2.93)
November	272	9.07 (2.19)
December	331	10.68 (4.26)
Total	3126	8.56 (3.21)

Data are mean (SD).

Table 1 presents the seasonal distribution and daily averages of AMI deaths for each season of the 12-month period.

The average daily AMI deaths in winter were 31.8% (9. 89 *v* 7.35, $p < 0.001$) higher than in summer. Table 2 shows monthly counts and daily averages of AMI deaths for each month; fig 1 illustrates the distribution of monthly AMI deaths, as a total and for each sex. The monthly maximum was recorded in December and the minimum in June. The average daily AMI deaths in June were 42.2% lower than December ($p < 0.001$) (table 2).

Figure 2A illustrates the proportion of each sex in AMI deaths for each age group (younger than 50 years, 50 to 70 years old and older than 70 years). It is evident that men die younger than women from AMI: only 13.9% were women in the age group below 50, whereas 47.5% of people older than 70 years dying of AMI were women. Figure 2B presents the monthly distribution of AMI deaths in each age group. Analysis of the mortality data for each age group showed that month-by-month variation is more pronounced for older people (mean daily count for AMI deaths of people older than 70 years was 3.53 in June and 7.03 in December; $p < 0.001$), whereas it is of marginal significance in people in their 50s and 60s (mean daily count for AMI deaths of people 50–70 years old was 2.17 in June and 3.13 in December; $p = 0.043$) and in younger people (mean daily count for AMI deaths of people younger than 50 years was 0.37 in June and 0.77 in November; $p = 0.049$). Analysis of variance between months for daily AMI deaths by age group showed that the variance was significant only in the age group older than 70 years (sum of squares for the 12 months in age groups less than 50, 50–70 and greater than 70 are 5.4 ($p = 0.473$), 20.2 ($p = 0.795$) and 330.3 ($p < 0.001$), respectively). If whole seasons are compared (winter *v* summer), only the age group of older than 70 years had a very significant differentiation (6.36 *v* 4.4, $p < 0.001$), whereas the age groups of 50–70 years (2.72 *v* 2.45, $p = 0.284$) and younger than 50 years (0.69 *v* 0.75, $p = 0.231$) had non-significant differences in daily AMI death counts between summer and winter.

Non-linear regression analysis of day-to-day data, with daily AMI deaths as the dependent variable, showed that the most powerful predictor of daily AMI deaths was the average temperature in the preceding seven days ($R^2 = 0.109$, $p < 0.001$). The relation between temperature and AMI mortality is U-shaped, with the minimum in daily AMI deaths corresponding to 23.3℃ (fig 3).

Forward linear regression analysis applied to monthly data indicated that mean monthly relative humidity values were independently correlated with monthly AMI deaths ($R = 0.764$, adjusted $R^2 = 0.541$, $p = 0.004$). The relation is linear and fig 4 depicts the curve.

DISCUSSION

The principal findings of the present study were as follows. Firstly, AMI deaths were seasonal, with the maximum mortality recorded in winter and the minimum in summer. Secondly, the observed seasonal variation of AMI deaths

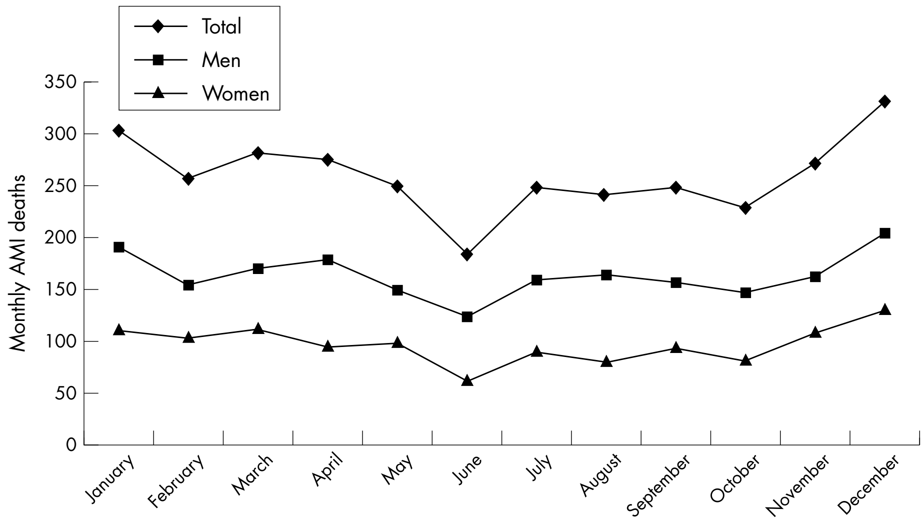

Figure 1 Distribution of monthly counts of deaths from acute myocardial infarction (AMI), in total and for each sex.

originated almost exclusively in the seasonal variation of AMI deaths in the elderly. Thirdly, the average mean temperature of the preceding seven days was the most powerfully associated (highest R^2) with daily AMI deaths. Lastly, monthly mean relative humidity values were independently correlated with monthly AMI deaths. Most studies of the relationship of climatic variables to mortality have used "cardiovascular mortality" or "ischaemic heart disease mortality" as end points, not providing data as to the specific causes of cardiovascular death (such as AMI, other coronary syndromes, embolisms and strokes). Our study used a much harder diagnosis as cause of death: AMI has well-defined diagnostic criteria and is usually readily recognised and adequately documented, whereas cardiovascular mortality leaves more room for misclassifications.

Athens is a metropolitan city with a temperate Mediterranean climate, with mild winters and long, hot summers. Our findings of increased cardiovascular mortality during winter months are in accordance with most of the previously published studies.[1–10] Winter mean daily AMI deaths were 31.8% higher than in summer, a figure strikingly similar to those previously reported: Kloner *et al*[7] reported 33% higher death rates from coronary artery disease in winter, van Rossum *et al*[9] recorded a 27% difference in death rates from ischaemic heart disease between January and July, and the Second National Registry of Myocardial Infarction survey reported 28–43% (depending on the geographical area) more AMIs in winter.[22] In our study, this temporal variation mostly concerned older people, as the difference

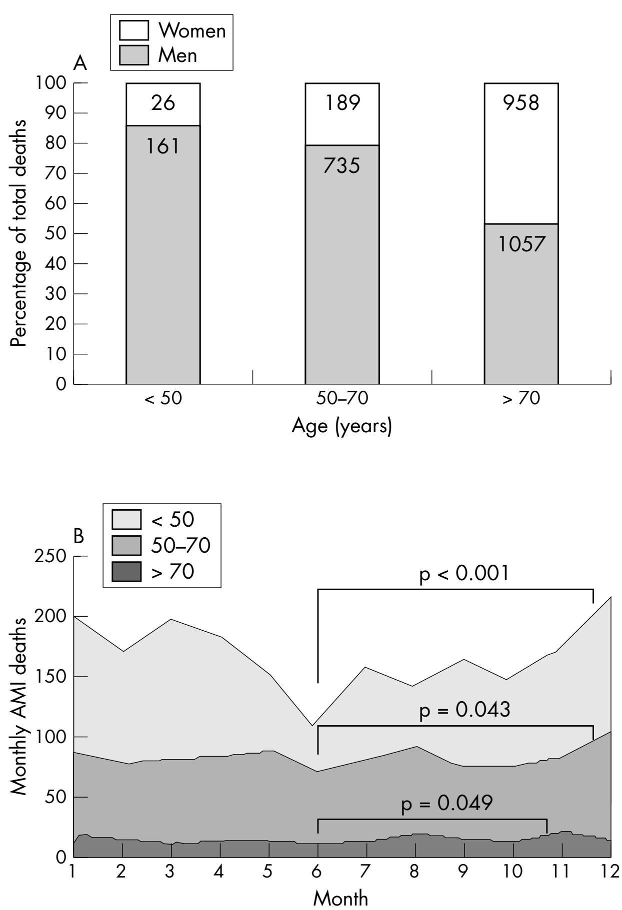

Figure 2 (A) Proportion of each sex in acute myocardial infarction (AMI) deaths for each age group (younger than 50 years, 50–70 years, older than 70 years). (B) Monthly distribution of AMI deaths in each age group (1 to 12 correspond to January, February, etc).

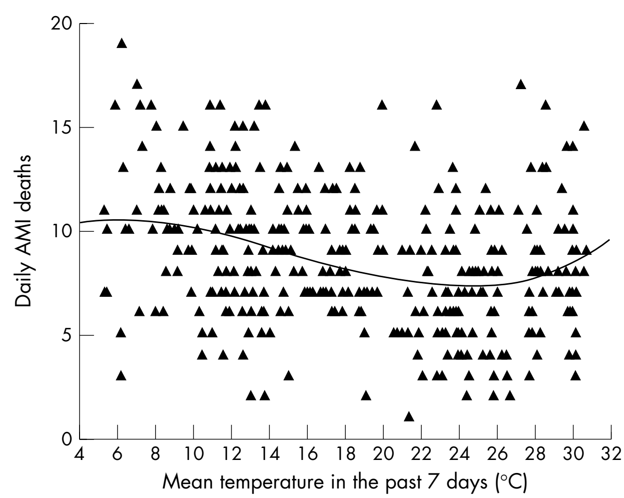

Figure 3 Scatter plot and fitted regression line of the association between daily acute myocardial infarction (AMI) deaths and the average mean daily temperatures of the previous seven days.

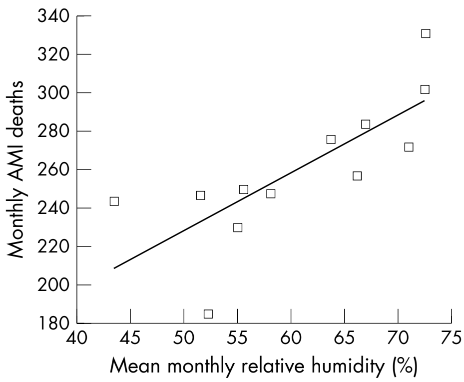

Figure 4 Scatter plot and fitted regression line of the association between monthly acute myocardial infarction (AMI) deaths and mean monthly relative humidity values.

between summer and winter was most pronounced for people older than 70 years and much less notable for younger people.

We found that the temperature–AMI mortality relation is U-shaped, indicating that, as temperature increases, the number of daily deaths declines, reaching a minimum corresponding to 23.3℃, then beginning to increase as the temperature rises. This finding agrees with previous reports.[18 20 23 24] The finding that the average of the mean daily temperatures of the preceding seven days was the best predictor of daily mortality suggests that temperature has a cumulative physiological effect, which indicates that consecutive days of low or high temperatures have more prominent an impact on AMI mortality than the mean temperature of a single day. The finding of a relative increase of AMI mortality during hot weather may indicate that, despite the efforts of the authorities to provide air-conditioned areas especially for older people on hot summer days, high temperatures still take their toll on older people.

The physiological mechanisms underlying the relationship between cold weather and cardiovascular events seem to be multifaceted. From a haemodynamic point of view, the stimulation of skin thermoreceptors results, through an increase in sympathetic activity and rise of plasma catecholamine concentrations, in peripheral vasoconstriction, tachycardia and increased blood pressure,[25 26] thus raising cardiac workload. In addition to these haemodynamic alterations, plasma fibrinogen and factor VIIc activity levels are higher in winter,[27] possibly indicating a cold-related hypercoagulable state, which favours thrombotic phenomena.[28] These responses to low temperatures probably constitute a substantial part of the pathophysiological interactions leading to increased rates of cardiovascular deaths in winter. Less studied is the relationship between high temperatures and cardiovascular mortality.

The relationship of ambient humidity to cardiovascular morbidity is unclear. Schwartz *et al*,[24] in a study across 12 US cities, found no consistent relationship between ambient humidity and hospital admissions for cardiovascular diseases. On the other hand, Panagiotakos *et al*,[17] in a study of emergency room admissions for non-fatal acute coronary syndromes in the Athens area, found a correlation with relative humidity. To the best of our knowledge, the present study is the first to identify a relationship between relative humidity and AMI deaths. This relationship between monthly mean values of relative humidity and monthly AMI death rates was the only statistically important one in the regression model to which temperature and atmospheric pressure parameters were added. The biological substrate of this relationship is unclear. In temperate climates with less pronounced winter–summer temperature differences, relative humidity possibly has a more influential effect on cardiovascular mortality than that previously recognised. That this correlation is evident only in the monthly analysis of the data may suggest that the impact of relative humidity on AMI mortality is exerted over a broader range of time than that of temperature. More studies are needed to verify these findings and, possibly, affirm the relatively strong association between excess environmental humidity and cardiovascular mortality.

As far as atmospheric pressure is concerned, our data did not show any significant correlation with AMI deaths, contrary to the previous report of the World Health Organization MONICA (MONitoring trends and determinants In CArdiovascular disease) project in Lille,[15] which described a U-shaped relationship between atmospheric pressure and myocardial infarction incidence and mortality. This study was performed in a city with climatic conditions substantially different from those in Athens (Lille has a humid oceanic climate, as opposed to the dry Mediterranean climate of Athens), which may account for this difference in observations; however, this point deserves further research.

The findings of the present study, regarding the effects of ambient temperature on the day-to-day data and relative humidity on the monthly data, do not imply that these atmospheric variables are solely responsible for the observed seasonal distribution of AMI deaths. Such studies cannot plausibly account for other possible causes of seasonality, such as variations in physical exercise and eating habits. The markedly high incidence of AMI deaths in December, for example, may be partly attributable to the ''Merry Christmas Coronary'' phenomenon, as eloquently put by Kloner[29]—that is, a constellation of circumstances, ranging from delay in seeking medical help, to overeating, overdrinking and increased emotional stress associated with the holiday period, that, combined, lead to increased cardiac mortality at that time of year.[30] However, we believe that such specific circumstances cannot fully account for the pronounced seasonality of cardiovascular mortality and morbidity. In the case of the holiday period, for example, one would expect a similar peak, or at least a local maximum, in AMI deaths at the time of the Easter holidays (in April), which in Greece is celebrated with even more indulgence than Christmas and is associated with all the factors suggested to be responsible for the ''Merry Christmas Coronary'' phenomenon, apart from the weather conditions. We did not observe such a peak in the present study.

Study limitations

Our study did not assess atmospheric pollution variables, which may influence cardiovascular mortality in a seasonal manner (air pollution in Athens is heavier in winter than in summer[31]). However, although associations of various air pollution determinants with cardiovascular mortality[32 33] and morbidity[31] have been found, there is no established relationship to AMI deaths. In addition, in the largest surveys in this field, the authors do not report including air pollution in their analysis as a confounder.[15 19] Moreover, it should be noted that among the numerous air pollutants, particulate matter (PM) (and more specifically the finest of airborne particles: PM10 and PM2.5—that is, particles with an aerodynamic diameter of less than 10 μm and 2.5 μm, respectively) has been shown to be the most significant pollutant associated with acute cardiovascular events.[34–36] In fact, a large study of several US cities reported that airborne particles were the only air pollutant that independently affected daily deaths.[37] It has also been shown that in Athens, although total PM mass varies significantly between seasons, the differences in PM10 and PM2.5 between summer and winter are very small.[38] It is thus reasonable to suggest that their effect on AMI deaths should not have important seasonal variation.

Another possible confounder that we were not able to control for was influenza epidemics. However, an increase in temperature was associated with an increase in AMI deaths (U-shaped curve) in periods of the year not associated with influenza (July and August), possibly indicating that the observed seasonality of AMI deaths is not totally attributable to influenza infections. Still, this constitutes a true limitation of our analysis.

Study implications

The finding that the number of AMI deaths among the elderly was in December more than twofold the number in June indicates that educating the population of senior citizens about the hazards of exposure to cold is inadequate. It may also suggest that, although Athens is a modern city with mostly adequate housing and heating installations, unsatisfactory provisions for these factors for the elderly may be an issue. The relative increase in AMI deaths with higher temperatures in the summer (the right arm of the U shape of the AMI deaths–temperature curve; fig 3), observed in a quite temperate summer for Athens (maximum daily temperature did not exceed 39°C), suggests that a more effective policy of civil protection during hot weather is necessary. Lastly, including the association of relative humidity with AMI mortality may be necessary in healthcare and civil protection planning.

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